NON-TECHNICAL ABSTRACT

We have demonstrated that the growth of HIV-1 can be blocked by the use of antisense genes. Specifically, we at Enzo designed three antisense genes that interfere with the functioning of two HIV-1 genes essential for virus growth in human cells. In experiments performed outside the body, we tested the effectiveness of these three antisense genes by introducing them into cultured human cells and then exposing these cells to HIV-1. We found that the cells that were producing antisense RNA from these genes were resistant to infection and destruction by HIV-1. This resistance was a stable property of these cells, *i.e.*, they were resistant to repeated exposures to HIV-1. The presence of these three genes had no apparent deleterious effect on the cells as indicated by tests that showed the presence of normal levels of cell proteins that characterize these cells as immune cells. When tested separately each of the three antisense genes was effective, but the three together were more effective than any one alone.

In our proposed study, we will put these three antisense genes into blood cell-producing stem cells. These cells are present in blood and bone marrow where they serve as a reservoir of progenitor cells that divide and develop into T4 cells and other blood cells. In this way it is thought they provide a lifelong source for the replenishment of T4 and other blood cells that are lost through aging and other natural processes. Introduction of the antisense genes into these progenitor cells could thus provide a continuous and renewable supply of antisense-containing T4 cells that are resistant to destruction by HIV-1.

In the proposed studies blood cell-producing stem cells will be collected from the circulating blood of HIV-1-infected individuals. The genetic antisense genes will be introduced into each patient's stem cells in the laboratory, and the treated cells will then be introduced back into these patients. We will study the patients to determine that this procedure is safe. We will also monitor the cells in each patient's blood for the presence of functioning antisense genes for a period of several months. In this way we can determine the stability of the functioning antisense genes within the body. We will also compare two separate dosing protocols to see if one is better.